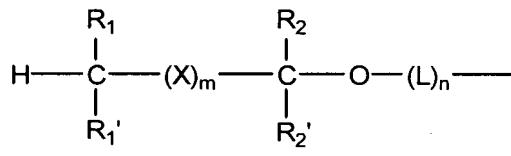


IN THE CLAIMS

Please amend claims 1, 5, 6, 16, and 22-24, as shown below. Please cancel claims 2-4 and 13 without prejudice. Please add new claims 25 – 41. The following listing of the claims replacing the previous claims.

1. (Currently amended) A method for treating a pathological condition of ocular tissue, comprising contacting a therapeutically active complex with ocular tissue, wherein the complex is formed by covalently attaching a moiety to a therapeutically active agent, resulting in a therapeutically active complex with low water solubility, thereby treating the condition, wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, retinal detachment caused by scratching and proliferation, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation, with the further proviso that the moiety is selected from a group consisting of sulfates, sulfonates, phosphates, lipids, phospholipids, carboxylates, sulfosuccinates, arginine esters, cholesterol esters, carbamates, carbonates, ketals, and the moiety having structure (I):



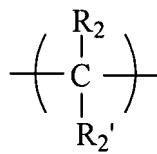
(I)

wherein:

each of R₁ and R_{1'} is independently selected from a group consisting of –H, an optionally substituted –O(C₁-C₂₄)alkyl, –O(C₁-C₂₄)alkenyl, –O(C₁-C₂₄)acyl, –S(C₁-C₂₄)alkyl, –S(C₁-C₂₄)alkenyl, and –S(C₁-C₂₄)acyl, wherein at least one of R₁ and R_{1'} is not –H, and wherein the alkenyl or acyl optionally has between 1 and 6 double bonds,

each of R₂ and R₂' is independently selected from a group consisting of -H, an optionally substituted -O(C₁-C₇)alkyl, -O(C₁-C₇)alkenyl, -S(C₁-C₇)alkyl, -S(C₁-C₇)alkenyl, -O(C₁-C₇)acyl, -S(C₁-C₇)acyl, -N(C₁-C₇)acyl, -NH(C₁-C₇)alkyl, -N((C₁-C₇)alkyl)₂, oxo, halogen, -NH₂, -OH, and -SH;

X is



L is selected from a group consisting of a valence bond and a bifunctional linking group of the formula -J-(CR₂)_t-G-, wherein t is an integer having the value between 1 and 24, each of J and G is independently selected from a group consisting of -O-, -S-, -C(O)O-, and -NH-, and R is selected from a group consisting of -H, substituted or unsubstituted alkyl, and alkenyl;

m is an integer having the value between 0 and 6; and

n is 0 or 1.

2-4. (Canceled).

5. (Currently amended) The method of claim 4 1, wherein m is selected from a group consisting of 0, 1, or 2.

6. (Currently amended) The method of claim 4 1, wherein m is 1.

7. (Original) The method of claim 1, wherein the complex has a particle size from about 10 nm up to 100,000 nm.

8. (Original) The method of claim 1, wherein the complex has a particle size from about 500 nm up to 100,000 nm.

9. (Original) The method of claim 1, wherein the complex has a particle size from about 500 nm up to about 50,000 nm.

10. (Original) The method of claim 1, wherein the complex is in a slurry comprising amorphous forms and crystalline forms.

11. (Original) The method of claim 1, wherein the complex is in substantially crystalline form.

12. (Original) The method of claim 1, wherein the complex is in substantially amorphous form.

13. (Canceled).

14. (Original) The method of claim 1, wherein the therapeutically active agent is an antiviral nucleoside.

15. (Original) The method of claim 14, wherein the antiviral nucleoside is adefovir, ganciclovir, cidofovir, cyclic cidofovir, or tenofovir.

16. (Currently amended) The method of claim 14, wherein the antiviral nucleoside is a derivative of azidothymidine (AZT).

17. (Original) The method of claim 1, wherein the therapeutically active agent is an anti-neoplastic nucleoside.

18. (Original) The method of claim 17, wherein the therapeutically active agent is a derivative of cytosine arabinoside, gemcitabine, 5-fluorodeoxyuridine riboside, 5-fluorodeoxyuridine deoxyriboside, 2-chlorodeoxyadenosine, fludarabine, or 1- β -D-arabinofuranosyl-guanine.

19. (Original) The method of claim 1, wherein the therapeutic agent is an antibody or a fragment thereof.

20. (Original) The method of claim 19, wherein the antibody is a polyclonal, a monoclonal, a chimeric, a single chain, or a humanized antibody.

21. (Original) The method of claim 19, wherein the antibody is a Fab fragment.

22. (Currently amended) A method for treating a pathological condition of ocular tissue, comprising administering to a subject in need thereof an effective amount of at least one complex of a therapeutically active agent, wherein the complex ~~of the therapeutically active agent has low water solubility and a~~ comprises particles having size in the range of ~~between~~ about 10 nm ~~to~~ and about 100,000 nm, thereby treating the pathological condition, ~~wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, retinal detachment caused by scratching and proliferation, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation.~~

23. (Currently amended) A method for the slow-release delivery of a therapeutically active agent to ocular tissue, comprising contacting the ocular tissue with a complex of a therapeutically active agent, wherein the complex ~~of the therapeutically active agent has low water solubility and a~~ comprises particles having size in the range of ~~between~~ about 10 nm ~~to~~ and about 100,000 nm, thereby delivering a slow-release therapeutically active agent to ocular tissue, ~~wherein the delivery of the agent is provided for the treatment or prevention of a pathological condition selected from a group consisting of macular degeneration, eye trauma, retinal detachment caused by scratching and proliferation, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation.~~

24. (Currently amended) A method for increasing residence time of a therapeutically active agent in ocular tissue, comprising covalently attaching a ~~the~~ moiety of claim 1 to the therapeutically active agent to form a complex ~~having low water solubility, providing the complex in a~~ comprising particles having size range between

In Re Application Of:

Hostetler et al.

Application No.: 10/770,885

Filed: February 2, 2004

Page 6

PATENT

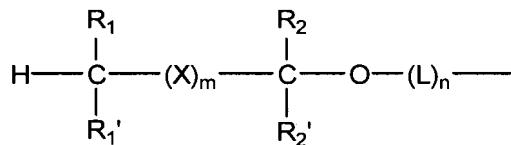
Attorney Docket No.: UCSD1480-1

about 10 nm to and about 100,000 nm, and contacting the complex with ocular tissue, thereby increasing residence time of a therapeutically active agent in ocular tissue.

25. (New) The method of any one of claims 1, 22, or 23, wherein the pathological condition is selected from a group consisting of macular degeneration and eye trauma.

26. (New) The method of any one of claims 1, 22, or 23, wherein the pathological condition is eye trauma.

27. (New) A method for treating a pathological condition of ocular tissue, comprising contacting a therapeutically active complex with ocular tissue, wherein the complex is formed by covalently attaching a moiety to a therapeutically active agent selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof, thereby treating the condition, wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, or retinal detachment, with the further proviso that the moiety is selected from a group consisting of sulfates, sulfonates, phosphates, lipids, phospholipids, carboxylates, sulfosuccinates, arginine esters, cholesterol esters, carbamates, carbonates, ketals, and the moiety having structure (I):



(I)

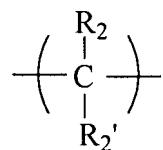
wherein:

each of R1 and R1' is independently selected from a group consisting of -H, an optionally substituted -O(C1-C24)alkyl, -O(C1-C24)alkenyl, -O(C1-C24)acyl,

—S(C1-C24)alkyl, —S(C1-C24)alkenyl, and —S(C1-C24)acyl, wherein at least one of R1 and R1' is not —H, and wherein the alkenyl or acyl optionally has between 1 and 6 double bonds,

each of R2 and R2' is independently selected from a group consisting of —H, an optionally substituted —O(C1-C7)alkyl, —O(C1-C7)alkenyl, —S(C1-C7)alkyl, —S(C1-C7)alkenyl, —O(C1-C7)acyl, —S(C1-C7)acyl, —N(C1-C7)acyl, —NH(C1-C7)alkyl, —N((C1-C7)alkyl)2, oxo, halogen, —NH2, —OH, and —SH;

X is



L is selected from a group consisting of a valence bond and a bifunctional linking group of the formula —J—(CR2)t—G—, wherein t is an integer having the value between 1 and 24, each of J and G is independently selected from a group consisting of —O—, —S—, —C(O)O—, and —NH—, and R is selected from a group consisting of —H, substituted or unsubstituted alkyl, and alkenyl;

m is an integer having the value between 0 and 6; and

n is 0 or 1.

28. (New) The method of claim 27, wherein m is selected from a group consisting of 0, 1, or 2.

29. (New) The method of claim 27, wherein m is 1.

30. (New) The method of claim 27, wherein the complex has a particle size from about 10 nm up to 100,000 nm.

31. (New) The method of claim 27, wherein the complex has a particle size from about 500 nm up to 100,000 nm.

32. (New) The method of claim 27, wherein the complex has a particle size from about 500 nm up to about 50,000 nm.

33. (New) The method of claim 27, wherein the complex is in a slurry comprising amorphous forms and crystalline forms.

34. (New) The method of claim 27, wherein the complex is in substantially crystalline form.

35. (New) The method of claim 27, wherein the complex is in substantially amorphous form.

36. (New) The method of claim 27, wherein the an anti-neoplastic nucleoside is a derivative of cytosine arabinoside, gemcitabine, 5-fluorodeoxyuridine riboside, 5-fluorodeoxyuridine deoxyriboside, 2-chlorodeoxyadenosine, fludarabine, or 1- β -D-arabinofuranosyl-guanine.

37. (New) The method of claim 27, wherein the antibody is a polyclonal, a monoclonal, a chimeric, a single chain, or a humanized antibody.

38. (New) The method of claim 37, wherein the antibody is a Fab fragment.

39. (New) A method for treating a pathological condition of ocular tissue, comprising administering to a subject in need thereof an effective amount of at least one complex of a therapeutically active agent, wherein the complex comprises particles having size between about 10 nm and about 100,000 nm, thereby treating the pathological condition, wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, or retinal detachment, with the further proviso that the therapeutically active agent is selected from a group consisting of

In Re Application Of:
Hostetler et al.
Application No.: 10/770,885
Filed: February 2, 2004
Page 9

PATENT
Attorney Docket No.: UCSD1480-1

adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.

40. (New) A method for the slow-release delivery of a therapeutically active agent to ocular tissue, comprising contacting the ocular tissue with a complex of a therapeutically active agent, wherein the complex comprises particles having size between about 10 nm and about 100,000 nm, thereby delivering a slow-release therapeutically active agent to ocular tissue, wherein the delivery of the agent is provided for the treatment or prevention of a pathological condition selected from a group consisting of macular degeneration, eye trauma, or retinal detachment, with the further proviso that the therapeutically active agent is selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.

41. (New) A method for increasing residence time of a therapeutically active agent in ocular tissue, comprising covalently attaching the moiety of claim 1 to the therapeutically active agent to form a complex comprising particles having size between about 10 nm and about 100,000 nm, and contacting the complex with ocular tissue, thereby increasing residence time of a therapeutically active agent in ocular tissue, with the further proviso that the therapeutically active agent is selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.